

Development of an Intravascular Laser Treatment with an Infrared Free Electron Laser

Selective Removal of Cholesterol Ester in Carotid Atheromatous Plaques

Y. NAKAJIMA, K. IWATSUKI, K. ISHII, T. FUJINAKA, K. AWAZU, T. YOSHIMINE

*Dept of Neurosurgery, Osaka University Medical School and Institute of Free Electron Laser,
Dept of Electronic, Information Systems and Energy Engineering, Graduate School of Engineering, Osaka University; Japan*

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Summary

We have studied to develop an intravascular device with an infrared free electron laser (FEL) to treat occlusive carotid atherosclerotic lesions. In this study, we irradiated the FEL with a wavelength of 5.75 μm on surgical specimens of human atheromatous carotid plaques. After the irradiation on a cholesterol-ester-accumulated portion of the carotid plaques under proper conditions, a microscope transmission FTIR (Fourier Transform Infrared) spectroscopy showed that the peak of a tissue infrared absorption spectrum corresponding to the molecular vibration of cholesterol ester (5.75 μm) disappeared. Tissue damages associated with the irradiation were not histologically noted. This study demonstrated that irradiation of FEL can selectively remove cholesterol ester from the human atheromatous carotid plaques.

Introduction

Infrared free electron lasers (FEL) are finding promising applications in a broad range of fields, including basic research into condensed matter physics, medicine and bioscience, nuclear energy and electronics. FEL uses also have been reported in medicine¹⁻³. We evaluated treatments of obstructive carotid artery diseases based on methods employing FEL.

The primary component of arterial atheromatous plaques is cholesterol ester, an ester bound combination of cholesterol and fatty acids, including oleic and linoleic acids. Irradiation by FEL with a wavelength that corresponds to the molecular vibration of this ester bond (5.75 μm) is reported to selectively degrade and eliminate cholesterol esters^{4,5}. We evaluated how this interaction with infrared FEL would provide low invasion and preventive treatment of atherosclerotic lesions in the carotid artery. An intravascular FEL treatment was developed to selectively remove cholesterol esters deposited in arteriosclerotic plaques.

Experimental Studies

We applied FEL irradiation to slices of human arterial atherosclerosis and evaluated the effectiveness of selective removal of cholesterol esters by changes in the infrared absorption spectra using microscopic transmission FTIR (Fourier Transform Infrared) spectroscopy. The peak in the infrared absorption spectrum derived from the intermolecular stretching vibration specific to an ester bond of cholesterol ester exists near 5.75 μm ⁶⁻⁸.

Laser light with a wavelength of 5.75 μm and power density of 15.9 W/cm^2 was used to irradiate intimal slices of extracted human arterial

atherosclerotic plaques. Peak signals derived from an ester bond of cholesterol ester decreased in height with irradiation time, and disappeared after 180 s. No other changes were observed in infrared absorption spectrum at 180 s of irradiation and no histological damage was noted.

Discussion

Laser angioplasty devices using conventional lasers have been used clinically to re-open obstructions in the coronary and peripheral arteries. These lasers are generated using light that is emitted (stimulated emission) when a specific energy level of lasing medium (YAG crystal, CO₂, etc.) is forced into continuous inversion and electrons in an excited state fall to a lower energy level.

Therefore, they are continuous waves (CW) with a specific wavelength determined by the lasing medium. Conventional intravascular laser treatments are used for degradation, ablation or emulsification of thrombi and atherosclerotic plaques, and application to cerebral vessels is difficult⁹⁻¹¹.

We have developed intravascular laser treatment using infrared FEL to selectively eliminate cholesterol ester deposition in atherosclerotic plaques. FEL uses synchrotron irradiation as the light source that is emitted when electrically charged electrons from a linear accelerator are forced to wiggle while passing through an undulator. There is a range of wavelengths due to differences in particle speed. Therefore, an FEL, emitted as a pulsed laser with high peak power, can be obtained by synchronizing the laser beam. Adjustment of the irradiation source and a linear accelerator settings, and strength of the magnetic field in the undulator enables arbitrary wavelengths to be generated across a broad range, including the infrared region. Devices in the Institute of Free Electron Laser, Osaka University, FEL covers a wide range of wavelengths: between 35 μm and 40 μm ¹²⁻¹⁴.

Infrared FEL exploits the specific IR sensitivity of biological molecules, such as proteins, sugar chains and lipids, which allows the regulation and the analysis, both structural and functional, of a target biomolecule. Irradiation by an infrared FEL with the chosen wavelength excites the corresponding biomolecular site to

enable regulation of various chemical reactions. Our purpose in this study was to selectively degrade cholesterol esters, the primary component of arterial atheromatous plaques, using FEL.

The ester bond between oleic acid and cholesterol in the cholesterol ester has a particular stretching vibration at 5.75 μm . Awazu et Al demonstrated that irradiation of atherosclerotic vessels in rabbits with FEL light at this wavelength degraded and eliminated cholesterol esters selectively⁴. However, a FEL irradiation at a 6.1 μm wavelength, equivalent to the stretching vibration of the amide I bond, protein abundant in the body, did not remove cholesterol esters selectively, but changed the peak of infrared absorption spectrum derived from amide I bonds and ablated elastic fibers of the blood vessels^{4,15}.

When FEL light was applied as a source of radiation to cholesterol esters and albumin films at wavelengths of 5.75 and 6.1 μm under certain conditions, 5.75 μm FEL resulted in degradation of cholesterol esters alone, and 6.1 μm light caused albumin ablation without cholesterol ester degradation⁵.

This study, as well as the above reports, shows that cholesterol esters contained in human carotid atheromatous plaques can be selectively eliminated using FEL light with a wavelength of 5.75 μm under appropriate conditions.

An intravascular technique to apply FEL irradiation to plaques may be a useful therapy. Stent implantation and percutaneous transluminal angioplasty have been used as intravascular treatments for obstructive lesions of the carotid artery¹⁶. Some countermeasures should be taken against distal embolization of soft plaques in vasodilatation of arteriosclerotic lesions. Although various devices have been developed to protect against embolisms, less invasive procedures are more desirable because atherosclerotic lesions in the vessels are usually highly advanced. A FEL is able to selectively degrade cholesterol esters, primary constituents of atheromatous plaques, without damaging other tissues. It shows promise as a low invasion technique, particularly on soft plaques that can cause distal embolism.

Atherosclerosis in the neck region is often a heterogeneous disease, with associated bleeding and calcification. Further investigation is

needed on the effects of FEL irradiation using more clinically representative samples. A thin, flexible laser fiber that can pass through a guiding catheter for intravascular treatment also needs to be developed^{4,17}.

We plan to conduct animal studies to investigate irradiation method in the body.

Conclusions

We have developed an intravascular infrared FEL laser treatment to remove cholesterol esters deposited in atherosclerotic plaques. Cholesterol esters in carotid plaques can be selectively eliminated using FEL with a wavelength of 5.75 μm under appropriate conditions.

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Yoshikazu Nakajima, M.D.
Department of Neurosurgery
Osaka University Medical School
2-2 Yamadaoka, Suita
Osaka 565-0871, Japan